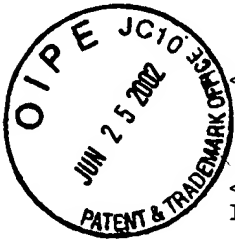


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<110> Samelson, Lawrence E.
Zhang, Weiguo

<120> The Protein Tyrosine Kinase Substrate LAT and Its Use in the Identification of (ANT) Agonists of the Kinase

<130> NIH-05065

<140> 09/597,920

<141> 2000-06-19

<150> PCT/US98/27400

<151> 1998-12-23

<160> 19

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35 40 45

Ile Gln Phe Lys Arg Pro His Thr Val Ala Pro Trp Pro Pro Ala Tyr
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Pro Pro Val Thr Ser Tyr Pro Pro Leu Ser Gln Pro Asp Leu Leu Pro
65 70 75 80

Ile Pro Arg Ser Pro Gln Pro Leu Gly Gly Ser His Arg Thr Pro Ser
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Ser Arg Arg Asp Ser Asp Gly Ala Asn Ser Val Ala Ser Tyr Glu Asn
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Glu Glu Pro Ala Cys Glu Asp Ala Asp Glu Asp Glu Asp Asp Tyr His
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Asn Pro Gly Tyr Leu Val Val Leu Pro Asp Ser Thr Pro Ala Thr Ser
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Thr Ala Ala Pro Ser Ala Pro Ala Leu Ser Thr Pro Gly Ile Arg Asp
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Ser Ala Phe Ser Met Glu Ser Ile Asp Asp Tyr Val Asn Val Pro Glu
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Ser Gly Glu Ser Ala Glu Ala Ser Leu Asp Gly Ser Arg Glu Tyr Val
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Asn Val Ser Gln Glu Leu His Pro Gly Ala Ala Lys Thr Glu Pro Ala
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Ser Ile Leu Ile Lys Pro Pro Gln Ile Thr Val Pro Arg Thr Pro Ala
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Val Ser Tyr Pro Leu Val Thr Ser Phe Pro Pro Leu Arg Gln Pro Asp
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Leu Leu Pro Ile Pro Arg Ser Pro Gln Pro Leu Gly Gly Ser His Arg
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Met Pro Ser Ser Gln Gln Asn Ser Asp Asp Ala Asn Ser Val Ala Ser
 100 105 110

Tyr Glu Asn Gln Glu Pro Ala Cys Lys Asn Val Asp Ala Asp Glu Asp
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Glu Asp Asp Tyr Pro Asn Gly Tyr Leu Val Val Leu Pro Asp Ser Ser
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Pro Ala Ala Val Pro Val Val Ser Ser Ala Pro Val Pro Ser Asn Pro
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Asp Leu Gly Asp Ser Ala Phe Ser Val Glu Ser Cys Glu Asp Tyr Val
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Asn Val Pro Glu Ser Glu Glu Ser Ala Glu Ala Ser Leu Asp Gly Ser
 180 185 190

Arg Glu Tyr Val Asn Val Ser Pro Glu Gln Gln Pro Val Thr Arg Ala
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<213> Homo sapiens

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Ser Leu Val Asp Asp Val Arg Phe His His Phe Pro Ile Glu Arg Gln
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Leu Asn Gly Thr Tyr Ala Ile Ala Gly Gly Lys Ala His Cys Gly Pro
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Ala Glu Leu Cys Gln Phe Tyr Ser Gln Asp Pro Asp Gly Leu Pro Cys
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Lys Glu Gln Gly Thr Tyr Ala Leu Ser Leu Val Tyr Gly Lys Thr Val
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Tyr His Tyr Leu Ile Ser Gln Asp Lys Ala Gly Lys Tyr Cys Ile Pro
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 Val Ser Asn Val Ala Glu Leu Leu His Gln Val Ala Met Gly Met Lys
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Gly Gly Phe Ala Leu Ser Val Ala His Gly Arg Lys Ala His His Tyr
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Thr Ile Glu Arg Glu Leu Asn Gly Thr Tyr Ala Ile Ala Gly Gly Arg
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Thr His Ala Ser Pro Ala Asp Leu Cys His Tyr His Ser Gln Glu Ser
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Asp Gly Leu Val Cys Leu Leu Lys Lys Pro Phe Asn Arg Pro Gln Gly
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Val Gln Pro Lys Thr Gly Pro Phe Glu Asp Leu Lys Glu Asn Leu Ile
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Arg Glu Tyr Val Lys Gln Thr Trp Asn Leu Gln Gly Gln Ala Leu Glu
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Gln Ala Ile Ile Ser Gln Lys Pro Gln Leu Glu Lys Leu Ile Ala Thr
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Thr Ala His Glu Lys Met Pro Trp Phe His Gly Lys Ile Ser Arg Glu
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His Glu Gly Lys Val Leu His Tyr Arg Ile Asp Lys Asp Lys Thr Gly
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Lys Leu Ser Ile Pro Glu Gly Lys Lys Phe Asp Thr Leu Trp Gln Leu
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Val Glu His Tyr Ser Tyr Lys Ala Asp Gly Leu Leu Arg Val Leu Thr
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Arg Pro Gln Leu Pro Gly Ser His Pro Ala Ser Ser Pro Ala Gln Gly
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Asn Arg Gln Glu Ser Thr Val Ser Phe Asn Pro Tyr Glu Pro Glu Leu
290 295 300

Ala Pro Trp Ala Ala Asp Lys Gly Pro Gln Arg Glu Ala Leu Pro Met
305 310 315 320

Asp Thr Glu Val Tyr Glu Ser Pro Tyr Ala Asp Pro Glu Glu Ile Arg
325 330 335

Pro Lys Glu Val Tyr Leu Asp Arg Lys Leu Leu Thr Leu Glu Asp Lys
340 345 350

Glu Leu Gly Ser Gly Asn Phe Gly Thr Val Lys Lys Gly Tyr Tyr Gln
355 360 365

Met Lys Lys Val Val Lys Thr Val Ala Val Lys Ile Leu Lys Asn Glu
370 375 380

Ala Asn Asp Pro Ala Leu Lys Asp Glu Leu Leu Ala Glu Ala Asn Val
385 390 395 400

Met Gln Gln Leu Asp Asn Pro Tyr Ile Val Arg Met Ile Gly Ile Cys
405 410 415

Glu Ala Glu Ser Trp Met Leu Val Met Glu Met Ala Glu Leu Gly Pro
420 425 430

Leu Asn Lys Tyr Leu Gln Gln Asn Arg His Val Lys Asp Lys Asn Ile
435 440 445

Ile Glu Leu Val His Gln Val Ser Met Gly Met Lys Tyr Leu Glu Glu
450 455 460

Ser Asn Phe Val His Arg Asp Leu Ala Ala Arg Asn Val Leu Leu Val
465 470 475 480

Thr Gln His Tyr Ala Lys Ile Ser Asp Phe Gly Leu Ser Lys Ala Leu
485 490 495

Arg Ala Asp Glu Asn Tyr Tyr Lys Ala Gln Thr His Gly Lys Trp Pro
500 505 510

Val Lys Trp Tyr Ala Pro Glu Cys Ile Asn Tyr Tyr Lys Phe Ser Ser
515 520 525

Lys Ser Asp Val Trp Ser Phe Gly Val Leu Met Trp Glu Ala Phe Ser
530 535 540

Tyr Gly Gln Lys Pro Tyr Arg Gly Met Lys Gly Ser Glu Val Thr Ala
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Met Leu Glu Lys Gly Glu Arg Met Gly Cys Pro Ala Gly Cys Pro Arg
565 570 575

Glu Met Tyr Asp Leu Met Asn Leu Cys Trp Thr Tyr Asp Val Glu Asn
580 585 590

Arg Pro Gly Phe Ala Ala Val Glu Leu Arg Leu Arg Asn Tyr Tyr Tyr
595 600 605

Asp Val Val Asn
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<210> 10

<211> 1109

<212> DNA

<213> Homo sapiens

<400> 10

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gacgagctga gcttcaaaag gggggacatc ctcaagggtt tgaacgaaga atgtgatcag 180

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<210> 11

<211> 217

<212> PRT

<213> Homo sapiens

<400> 11

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Leu Ser Phe Lys Arg Gly Asp Ile Leu Lys Val Leu Asn Glu Glu Cys
20 25 30

Asp Gln Asn Trp Tyr Lys Ala Glu Leu Asn Gly Lys Asp Gly Phe Ile
35 40 45

Pro Lys Asn Tyr Ile Glu Met Lys Pro His Pro Trp Phe Phe Gly Lys
50 55 60

Ile Pro Arg Ala Lys Ala Glu Glu Met Leu Ser Lys Gln Arg His Asp
65 70 75 80

Gly Ala Phe Leu Ile Arg Glu Ser Glu Ser Ala Pro Gly Asp Phe Ser
85 90 95

Leu Ser Val Lys Phe Gly Asn Asp Val Gln His Phe Lys Val Leu Arg
100 105 110

Asp Gly Ala Gly Lys Tyr Phe Leu Trp Val Val Lys Phe Asn Ser Leu
115 120 125

Asn Glu Leu Val Asp Tyr His Arg Ser Thr Ser Val Ser Arg Asn Gln
130 135 140

Gln Ile Phe Leu Arg Asp Ile Glu Gln Val Pro Gln Gln Pro Thr Tyr
145 150 155 160

Val Gln Ala Leu Phe Asp Phe Asp Pro Gln Glu Asp Gly Glu Leu Gly
165 170 175

Phe Arg Arg Gly Asp Phe Ile His Val Met Asp Asn Ser Asp Pro Asn
180 185 190

Trp Trp Lys Gly Ala Cys His Gly Gln Thr Gly Met Phe Pro Arg Asn
195 200 205

Tyr Val Thr Pro Val Asn Arg Asn Val
210 215

<210> 12

<211> 2757

<212> DNA

<213> Homo sapiens

<400> 12

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gctactgggc tatctggaca agggaaaacg caagcgcaaa gagaaagcag ttctgtgcc	180
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cgggtggagga ggatgaggac ctgtatgact gcgtggagaa tgaggaggcg gaaggcgacg	480
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<210> 13

<211> 797

<212> PRT

<213> Homo sapiens

<400> 13

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Lys Arg Lys Gln Phe Leu Cys Leu Lys Asn Ile Arg Thr Phe Leu Ser
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Thr Cys Cys Glu Lys Phe Gly Leu Lys Arg Ser Glu Leu Phe Glu Ala
35 40 45

Phe Asp Leu Phe Asp Val Gln Asp Phe Gly Lys Val Ile Tyr Thr Leu
50 55 60

Ser Ala Leu Ser Trp Thr Pro Ile Ala Gln Asn Arg Gly Ile Met Pro
65 70 75 80

Phe Pro Thr Glu Glu Glu Ser Val Gly Asp Glu Asp Ile Tyr Ser Gly
85 90 95

Leu Ser Asp Gln Ile Asp Asp Thr Val Glu Glu Asp Glu Asp Leu Tyr
100 105 110

Asp Cys Val Glu Asn Glu Glu Ala Glu Gly Asp Glu Ile Tyr Glu Asp
115 120 125

Leu Met Arg Ser Glu Pro Val Ser Met Pro Pro Lys Met Thr Glu Tyr
130 135 140

Asp Lys Arg Cys Cys Cys Leu Arg Glu Ile Gln Gln Thr Glu Glu Lys
145 150 155 160

Tyr Thr Asp Thr Leu Gly Ser Ile Gln Gln His Phe Leu Lys Pro Leu
 165 170 175
 Gln Arg Phe Leu Lys Pro Gln Asp Ile Glu Ile Ile Phe Ile Asn Ile
 180 185 190
 Glu Asp Leu Leu Arg Val His Thr His Phe Leu Lys Glu Met Lys Glu
 195 200 205
 Ala Leu Gly Thr Pro Gly Ala Pro Asn Leu Tyr Gln Val Phe Ile Lys
 210 215 220
 Tyr Lys Glu Arg Phe Leu Val Tyr Gly Arg Tyr Cys Ser Gln Val Glu
 225 230 235 240
 Ser Ala Ser Lys His Leu Asp Arg Val Ala Ala Ala Arg Glu Asp Val
 245 250 255
 Gln Met Lys Leu Glu Glu Cys Ser Gln Arg Ala Asn Asn Gly Arg Phe
 260 265 270
 Thr Ala Arg Pro Ala Asp Gly Ala Tyr Ala Ala Ser Ser Gln Ile Ser
 275 280 285
 Pro Pro Ser Pro Gly Ala Gly Glu Thr His Ala Gly Gly Asp Gly Ala
 290 295 300
 Arg Lys Leu Arg Leu Ala Leu Asp Ala Met Arg Asp Leu Ala Gln Cys
 305 310 315 320
 Val Asn Glu Val Lys Arg Asp Asn Glu Thr Leu Arg Gln Ile Thr Asn
 325 330 335
 Phe Gln Leu Ser Ile Glu Asn Leu Asp Gln Ser Leu Ala His Tyr Gly
 340 345 350
 Arg Pro Lys Ile Asp Gly Glu Leu Lys Ile Thr Ser Val Glu Arg Arg
 355 360 365
 Ser Lys Met Asp Arg Tyr Ala Phe Leu Leu Asp Lys Ala Leu Leu Ile
 370 375 380
 Cys Lys Arg Arg Gly Asp Ser Tyr Asp Leu Lys Asp Phe Val Asn Leu
 385 390 395 400
 His Ser Phe Gln Val Arg Asp Asp Ser Ser Gly Asp Arg Asp Asn Lys
 405 410 415

Lys Trp Ser His Met Phe Leu Leu Ile Glu Asp Gln Gly Ala Gln Gly
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Tyr Glu Leu Phe Phe Lys Thr Arg Glu Leu Lys Lys Lys Trp Met Glu
435 440 445

Gln Phe Glu Met Ala Ile Ser Asn Ile Tyr Pro Glu Asn Ala Thr Ala
450 455 460

Asn Gly His Asp Phe Gln Met Phe Ser Phe Glu Glu Thr Thr Ser Cys
465 470 475 480

Lys Ala Cys Gln Met Leu Leu Arg Gly Thr Phe Tyr Gln Gly Tyr Arg
485 490 495

Cys His Arg Cys Arg Ala Ser Ala His Lys Glu Cys Leu Gly Arg Val
500 505 510

Pro Pro Cys Gly Arg His Gly Gln Asp Phe Pro Gly Thr Met Lys Lys
515 520 525

Asp Lys Leu His Arg Arg Ala Gln Asp Lys Lys Arg Asn Glu Leu Gly
530 535 540

Leu Pro Lys Met Glu Val Phe Gln Glu Tyr Tyr Gly Leu Pro Pro Pro
545 550 555 560

Pro Gly Ala Ile Gly Pro Phe Leu Arg Leu Asn Pro Gly Asp Ile Val
565 570 575

Glu Leu Thr Lys Ala Glu Ala Glu Gln Asn Trp Trp Glu Gly Arg Asn
580 585 590

Thr Ser Thr Asn Glu Ile Gly Trp Phe Pro Cys Asn Arg Val Lys Pro
595 600 605

Tyr Val His Gly Pro Pro Gln Asp Leu Ser Val His Leu Trp Tyr Ala
610 615 620

Gly Pro Met Glu Arg Ala Gly Ala Glu Ser Ile Leu Ala Asn Arg Ser
625 630 635 640

Asp Gly Thr Phe Leu Val Arg Gln Arg Val Lys Asp Ala Ala Glu Phe
645 650 655

Ala Ile Ser Ile Lys Tyr Asn Val Glu Val Lys His Thr Val Lys Ile
660 665 670

Met Thr Ala Glu Gly Leu Tyr Arg Ile Thr Glu Lys Lys Ala Phe Arg
675 680 685

Gly Leu Thr Glu Leu Val Glu Phe Tyr Gln Gln Asn Ser Leu Lys Asp
690 695 700

Cys Phe Lys Ser Leu Asp Thr Thr Leu Gln Phe Pro Phe Lys Glu Pro
705 710 715 720

Glu Lys Arg Thr Ile Ser Arg Pro Ala Val Gly Ser Thr Lys Tyr Phe
725 730 735

Gly Thr Ala Lys Ala Arg Tyr Asp Phe Cys Ala Arg Asp Arg Ser Glu
740 745 750

Leu Ser Leu Lys Glu Gly Asp Ile Ile Lys Ile Leu Asn Lys Lys Gly
755 760 765

Gln Gln Gly Trp Trp Arg Gly Glu Ile Tyr Gly Arg Val Gly Trp Phe
770 775 780

Pro Ala Asn Tyr Val Glu Glu Asp Tyr Ser Glu Tyr Cys
785 790 795

<210> 14

<211> 3090

<212> DNA

<213> Homo sapiens

<400> 14

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<210> 15

<211> 896

<212> PRT

<213> Homo sapiens

<400> 15

Met Ala Gly Asn Val Lys Lys Ser Ser Gly Ala Gly Gly Gly Gly Ser
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Gly Gly Ser Gly Ala Gly Gly Leu Ile Gly Leu Met Lys Asp Ala Phe
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Gln Pro His His His His His His Leu Ser Pro His Pro Pro Cys Thr
35 40 45

Val Asp Lys Lys Met Val Glu Lys Cys Trp Lys Leu Met Asp Lys Val
50 55 60

Val Arg Leu Cys Gln Asn Pro Asn Val Ala Leu Lys Asn Ser Pro Pro
65 70 75 80

Tyr Ile Leu Asp Leu Leu Pro Asp Thr Tyr Gln His Leu Arg Thr Val
85 90 95

Leu Ser Arg Tyr Glu Gly Lys Met Glu Thr Leu Gly Glu Asn Glu Tyr
100 105 110

Phe Arg Val Phe Met Glu Asn Leu Met Lys Lys Thr Lys Gln Thr Ile
 115 120 125
 Ser Leu Phe Lys Glu Gly Lys Glu Arg Met Tyr Glu Glu Asn Ser Gln
 130 135 140
 Pro Arg Arg Asn Leu Thr Lys Leu Ser Leu Ile Phe Ser His Met Leu
 145 150 155 160
 Ala Glu Leu Lys Gly Ile Phe Pro Ser Gly Leu Phe Gln Gly Asp Thr
 165 170 175
 Phe Arg Ile Thr Lys Ala Asp Ala Ala Glu Phe Trp Arg Lys Ala Phe
 180 185 190
 Gly Glu Lys Thr Ile Val Pro Trp Lys Ser Phe Arg Gln Ala Leu His
 195 200 205
 Glu Val His Pro Ile Ser Ser Gly Leu Glu Ala Met Ala Leu Lys Ser
 210 215 220
 Thr Ile Asp Leu Thr Cys Asn Asp Tyr Ile Ser Val Phe Glu Phe Asp
 225 230 235 240
 Ile Phe Thr Arg Leu Phe Gln Pro Trp Ser Ser Leu Leu Arg Asn Trp
 245 250 255
 Asn Ser Leu Ala Val Thr His Pro Gly Tyr Met Ala Phe Leu Thr Tyr
 260 265 270
 Asp Glu Val Lys Ala Arg Leu Gln Lys Phe Ile His Lys Pro Gly Ser
 275 280 285
 Tyr Ile Phe Arg Leu Ser Cys Thr Arg Leu Gly Gln Trp Ala Ile Gly
 290 295 300
 Tyr Val Thr Ala Asp Gly Asn Ile Leu Gln Thr Ile Pro His Asn Lys
 305 310 315 320
 Pro Leu Phe Gln Ala Leu Ile Asp Gly Phe Arg Glu Gly Phe Tyr Leu
 325 330 335
 Phe Pro Asp Gly Arg Asn Gln Asn Pro Asp Leu Thr Gly Leu Cys Glu
 340 345 350
 Pro Thr Pro Gln Asp His Ile Lys Val Thr Gln Ile Cys Ala Glu Asn
 355 360 365

Asp Lys Asp Val Lys Ile Glu Pro Cys Gly His Leu Met Cys Thr Ser
370 375 380

Cys Leu Thr Ser Trp Gln Glu Ser Glu Gly Gln Gly Cys Pro Phe Cys
385 390 395 400

Arg Cys Glu Ile Lys Gly Thr Glu Pro Ile Val Val Asp Pro Phe Asp
405 410 415

Pro Arg Gly Ser Gly Ser Leu Leu Arg Gln Gly Ala Glu Gly Ala Pro
420 425 430

Ser Pro Asn Tyr Asp Asp Asp Asp Glu Arg Ala Asp Asp Ser Leu
435 440 445

Phe Met Met Lys Glu Leu Ala Gly Ala Lys Val Glu Arg Pro Ser Ser
450 455 460

Pro Phe Ser Met Ala Pro Gln Ala Ser Leu Pro Pro Val Pro Pro Arg
465 470 475 480

Leu Asp Leu Leu Gln Gln Arg Ala Pro Val Pro Ala Ser Thr Ser Val
485 490 495

Leu Gly Thr Ala Ser Lys Ala Ala Ser Gly Ser Leu His Lys Asp Lys
500 505 510

Pro Leu Pro Ile Pro Pro Thr Leu Arg Asp Leu Pro Pro Pro Pro Pro
515 520 525

Pro Asp Arg Pro Tyr Ser Val Gly Ala Glu Thr Arg Pro Gln Arg Arg
530 535 540

Pro Leu Pro Cys Thr Pro Gly Asp Cys Pro Ser Arg Asp Lys Leu Pro
545 550 555 560

Pro Val Pro Ser Ser Arg Pro Gly Asp Ser Trp Leu Ser Arg Thr Ile
565 570 575

Pro Lys Val Pro Val Ala Thr Pro Asn Pro Gly Asp Pro Trp Asn Gly
580 585 590

Arg Glu Leu Thr Asn Arg His Ser Leu Pro Phe Ser Leu Pro Ser Gln
595 600 605

Met Glu Pro Arg Ala Asp Val Pro Arg Leu Gly Ser Thr Phe Ser Leu
 610 615 620
 Asp Thr Ser Met Thr Met Asn Ser Ser Pro Val Ala Gly Pro Glu Ser
 625 630 635 640
 Glu His Pro Lys Ile Lys Pro Ser Ser Ser Ala Asn Ala Ile Tyr Ser
 645 650 655
 Leu Ala Ala Arg Pro Leu Pro Met Pro Lys Leu Pro Pro Gly Glu Gln
 660 665 670
 Gly Glu Ser Glu Glu Asp Thr Glu Tyr Met Thr Pro Thr Ser Arg Pro
 675 680 685
 Val Gly Val Gln Lys Pro Glu Pro Lys Arg Pro Leu Glu Ala Thr Gln
 690 695 700
 Ser Ser Arg Ala Cys Asp Cys Asp Gln Gln Ile Asp Ser Cys Thr Tyr
 705 710 715 720
 Glu Ala Met Tyr Thr Ile Gln Ser Gln Ala Leu Ser Val Ala Glu Asn
 725 730 735
 Ser Ala Ser Gly Glu Gly Asn Leu Ala Thr Ala His Thr Ser Thr Gly
 740 745 750
 Pro Glu Glu Ser Glu Asn Glu Asp Asp Gly Tyr Asp Val Pro Lys Pro
 755 760 765
 Pro Val Pro Ala Val Leu Ala Arg Arg Thr Leu Ser Asp Ile Ser Asn
 770 775 780
 Ala Ser Ser Ser Phe Gly Trp Leu Ser Leu Asp Gly Asp Pro Thr Asn
 785 790 795 800
 Phe Asn Glu Gly Ser Gln Val Pro Glu Arg Pro Pro Lys Pro Phe Pro
 805 810 815
 Arg Arg Ile Asn Ser Glu Arg Lys Ala Ser Ser Tyr Gln Gln Gly Gly
 820 825 830
 Gly Ala Thr Ala Asn Pro Val Ala Thr Ala Pro Ser Pro Gln Leu Ser
 835 840 845
 Ser Glu Ile Glu Arg Leu Met Ser Gln Gly Tyr Ser Tyr Gln Asp Ile
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Gln Lys Ala Leu Val Ile Ala His Asn Asn Ile Glu Met Ala Lys Asn
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